IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BOSTON SCIENTIFIC CORPORATION and BOSTON SCIENTIFIC SCIMED, INC.,	
Plaintiffs,	Civil Action No. 07-333-SLR Civil Action No. 07-348-SLR Civil Action No. 07-409-SLR
v.	
JOHNSON & JOHNSON, INC. and CORDIS CORPORATION	**REDACTED PUBLIC VERSION**
Defendants.	

DEFENDANTS/COUNTER-PLAINTIFFS JOHNSON & JOHNSON AND CORDIS'S OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT OF INVALIDITY OF THE '7286, '3286, AND '473 PATENTS-IN-SUIT PURSUANT TO 35 U.S.C.§ 103

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INTRODUCTION

BSC's motion for summary judgment that the asserted claims of Cordis's '3286, '7286 and '473 patents (the "'1997 patents") are invalid under 35 U.S.C. § 103 should be denied because BSC's obviousness defense depends on the resolution of many vigorously contested underlying issues of fact.[1]

The 1997 patents, as well as the later '662 patent, claim inventions used to create Cordis Corporation's pioneering Cypher® drug-eluting stent. By 1997, Cordis's invention of the bare metal stent had revolutionized the treatment of heart disease—the number one killer in the United States. But prior to the claimed inventions, restenosis (the renarrowing of arteries following stent implantation) remained the single most serious problem associated with stent technology. An army of medical device companies, drug companies, cardiologists and researchers tried to solve this problem with little success. A myriad of different drugs, devices, and approaches were tried, from atherectomy drills, to lasers, to radiation, to local drug delivery, but none solved the problem.

The problem was finally solved by Cordis, when its scientists put the right pieces together to create and develop the groundbreaking Cypher® stent – a stent that worked so well that it stunned the cardiology community. An article in the leading peer-reviewed cardiology journal *Circulation* gave one highly respected cardiologist's reaction to the Cypher® stent:

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[1] BSC also seeks summary judgment that Claims 1, 2, 5, 6, 40, 41, 44, 47 and 48 of U.S. Patent No. 7,223,286 are invalid. However, as set forth in pp. 17-18 of Defendants/Counter-Plaintiffs Johnson & Johnson and Cordis Corporation's Opposition to Plaintiff's Motion for Summary Judgment of Non-Infringement of the Asserted Claims of the '7286, '3286 and '473 patents-in-suit, BSC's motion for summary judgment regarding the validity of these claims is not justiciable and should be denied as moot.

> "If I am in a dream, please don't wake me" are the now-fabled words spoken by Patrick Serruys while viewing follow-up intravascular ultrasound images of [Cypher®] sirolimus-eluting stents. The dream of an effective treatment for restenosis has eluded decades of effort by an army of investigators. Scores of devices, hundreds of drugs, and innumerable revascularization "strategies" have failed to eliminate the 10% to 50% risk of recurrence after angioplasty.

The author continued:

> Despite the early nature of this report and the admonition to remain skeptical, it is hard for many of us who have witnessed the growth of interventional cardiology to contain our enthusiasm.[2]

The patents-in-suit represent key milestones in Cordis's development of the Cypher® stent. In the 1997 patents, the inventors claimed the combinations of key elements critical to the ultimate success of Cypher® – mixing the right drug (a rapamycin or macrocyclic lactone analogs thereof) in the right polymers (nonerodible polymers, including fluorinated polymers and acrylates) and coating them on a stent to achieve controlled release over a period of several weeks. After the Cypher® stent demonstrated the dramatic success of these inventions, others followed suit, including Abbott and BSC – the sellers of the Xience/Promus stent. Together, stents using Cordis's inventions account for the majority of the drug-eluting stents sold in the United States today.

Having adopted the invention of the 1997 patents, BSC now seeks to invalidate those patents. But BSC's motion creates numerous disputed issues of material fact including, *inter alia*, what is taught by the prior art as a whole, what is taught by the individual references, whether those references teach away from the claimed inventions, whether there would be a motivation to combine the references in a manner that would achieve the claimed inventions, and

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[2] Paul Teirstein, Living the Dream of No Restenosis, *Circulation*, 2001; 104:1996-1998 at 1996, (A2378).

the significance of the "secondary considerations" of nonobviousness, which BSC does not dispute for purposes of this motion. Cordis introduces detailed factual testimony, including declarations from a renowned biomaterials expert, Dr. Antonios Mikos, and cardiologist, Dr. Campbell Rogers, explaining how a person of ordinary skill in 1997 would understand these factual questions. BSC's responses, which rely on no declaration but only attorney argument, are insufficient to obviate these numerous fact issues. Summary judgment should be denied.

STAGE OF THE PROCEEDING

The stage of the present case is discussed in Cordis's Response Brief to Plaintiffs Motion for Summary Judgment of Invalidity Under 35 U.S.C. § 112.

SUMMARY OF ARGUMENT

1. BSC's obviousness defense is a classic use of impermissible hindsight, and there is ample evidence from which a jury could conclude that BSC failed to meet its burden of proving by clear and convincing evidence that the 1997 patents are invalid. By 1997, researchers were pursuing many different approaches to the intractable problem of restenosis, generating a vast array of prior art. But the problem remained unsolved.

2. Now, in hindsight, BSC cherry-picks particular statements from this vast array of prior art to try to cobble together the insights and inventions made by the Cordis inventors. Even these, however, fall far short, as they either point in different directions or simply contain lengthy laundry lists of drugs, polymers and medical devices that offer an almost infinite number of possible combinations. These lists would have provided no guidance to a person of ordinary skill in 1997 attempting to solve the problem of restenosis. BSC also ignores contemporaneous evidence teaching away from the use of the types of polymers on a stent that are used in the claimed inventions. Numerous disputed fact questions are created by declarations of experts that

squarely contradict BSC's factual assertions concerning the teachings of the prior art and the motivation to combine references.

3. BSC also ignores—and asks this Court to ignore—Cordis's powerful affirmative evidence of non-obviousness—the so called "secondary considerations"—which the Federal Circuit has held ***must*** be considered by the district court in assessing obviousness. Cordis has made an overwhelming factual showing of long-felt need, unexpected results, failed efforts of others, commercial success and industry recognition. Every one of these factors suggests, indeed compels, the conclusion that the claimed inventions were not obvious. This undisputed evidence is fatal to BSC's motion for summary judgment.

STATEMENT OF FACTS

1. The Long-Standing Problem of Restenosis

Prior to the advent of coronary angioplasty there was no effective treatment for coronary artery disease (CAD) other than open heart surgery, an enormously traumatic, painful, and risky procedure requiring an extended hospital stay and months of recovery time. Angioplasty, first used in 1977, involves inserting a balloon catheter in the groin area, threading it up to the site of the blockage, and expanding it to open the obstruction. This was a major advance because it was both effective and non-invasive, but in a large percentage of cases the blockage would reappear within six months—a process known as restenosis. Described as the "Achilles Heel" of the interventional cardiologist, restenosis profoundly limited the long-term success and usefulness of angioplasty. (Rogers Decl. at A10-A11 ¶ 30; Mikos Decl. at A94-A95 ¶ 21).

Restenosis was caused by three phenomena: vascular recoil (collapse of the artery following balloon deflation), negative remodeling (construction of the artery due to scarring), and neointimal proliferation (multiplication of cells in the artery causing it to narrow over time). (Rogers Decl. at A8-A9 ¶¶ 23-24; Mikos Decl. at A93-A94 ¶¶ 18-19). In the late 1980s,

Johnson & Johnson and Julio Palmaz, M.D., pioneered the development of bare metal stents to address the first two components of restenosis, and introduced the Palmaz-Shatz stent for coronary procedures in the United States in 1994. (Rogers Decl. at A9-A10 ¶¶ 25-29). Although these bare metal stents revolutionized the treatment of coronary artery disease, they did not address the third component of restenosis – neointimal proliferation, and thus did not entirely eliminate restenosis. (Rogers Decl. at A10-A11 ¶30, Mikos Decl. at A94-A95 ¶ 21). As a result, restenosis remained a major problem in interventional cardiology, resulting in restenosis rates of 20-30% in stent patients. (Rogers Decl. at A10-A11 ¶30, Mikos Decl. at A94-A95 ¶ 21). In the 1990s, finding a solution to the restenosis problem remained the Holy Grail of interventional cardiology.

2. The Numerous Failed Attempts By Others To Solve The Problem Of Restenosis

Before the Cypher® stent, scientists, cardiologists, drug companies, device companies and others desperately sought a lasting solution to the problem of restenosis. (Rogers Decl. at A13-A33 ¶¶ 39-75; Mikos Decl. at A155-A160 ¶¶ 199-207). It was far from clear that improving the performance of stents was possible or practical. So during the 1990s, a plethora of different approaches were proposed and tried with little success, including:

- Laser therapy: A catheter with an excimer laser at its tip was threaded through the artery to the site of blockage and activated to remove smooth muscle cells from the site of blockage. (Rogers Decl. at A14-A15 ¶¶ 44-45).
- Atherectomy: A small drill-like device was attached to a catheter, threaded to the site of blockage, and used to break up the blockage in the artery. (Rogers Decl. at A15-A16 ¶¶ 46-47).
- Cutting balloons: Microblades were mounted longitudinally on the surface of an angioplasty balloon which made small incisions into the arterial wall which was believed to result in less growth factor expression and neointimal proliferation. (Rogers Decl. at A16-A17 ¶¶ 48-49).

- Radiation catheters (brachytherapy): Radioactive seeds were delivered to the site of blockage to kill proliferating cells. Cumbersome efforts were required to protect the patient and the operating room staff from the harmful effects of radiation. (Rogers Decl. at A17-A18 ¶¶ 50-52).

- Radioactive stents: Stents were designed to emit radiation. (*Id.*)

- Local drug delivery from balloon: Drugs were stored in a balloon and sprayed out as the balloon inflated in the artery. (Rogers Decl. at A18 ¶ 53).

- Local drug delivery from double balloon catheter: Two balloons isolated the blockage and infused drug into the area. (Rogers Decl. at A18-A19 ¶ 54).

- Local drug delivery using ionotophoretic balloon catheters: Drug was delivered using a catheter relying on electric current to increase permeability and facilitate transport into the vessel wall. (Mikos Decl. at A158 ¶ 205).

- Oral or systemically delivered drugs: A multitude of drugs showed promise when delivered orally or systemically in animal models, including drugs preventing thrombus formation, vascular recoil and remodeling, antiproliferative and anti-inflammatory agents, and combinations of drugs. (Rogers Decl. at A19-A26 ¶¶ 56-60).

- Drug delivery from a stent: Numerous approaches were proposed, including dipping or spraying the drug on a stent, attaching the drug via a covalent bond, using a polymer stent, using a sheath on the outside of the stent, or using a variety of different types of polymer coatings. (Mikos Decl. at A159-160 ¶ 208; Rogers Decl. at A26-A33 ¶¶ 61-75).

None of these efforts solved the problem of restenosis. (Rogers Decl. at A26-A33 ¶¶ 61-75). By 1997, the failure to solve the problem was well-recognized and the subject of significant concern in the cardiology community. Leading researchers in a 1997 article noted that despite the "widespread intensive research effort" directed toward addressing restenosis, "the results have been almost uniformly disappointing." David Brieger & Eric Topol, Local Drug Delivery Systems and Prevention of Restenosis, *Cardio Res* 1997; 35(3):405-413 at 405, (A1410). A later presentation at the 1999 American College of Cardiology meeting further lamented that, despite the use of various devices to address restenosis, "late clinical outcomes after treatment of" restenosis "remain disappointing, and surprisingly independent of device choice." Mehran *et al.*,

In-Stent Restenosis: "The Great Equalizer" – Disappointing Clinical Outcomes with all Interventional Strategies. *J Am Coll Cardiol* 1999; 33 at 63A, (A1870). The authors further opined that "a definitive 'cure'" for restenosis "will require additional adjunct antiproliferative therapy, such as radiation vascular therapy which is under investigation."[3] *Id.*

3. The Numerous Failed Attempts By Others To Create A Drug-Eluting Stent

Prior to (and even after) the Cypher® stent, attempts by others to find the right combination for a drug-eluting stent fared little better than many other unsuccessful approaches. Companies and researchers devoted significant efforts to finding the right combination to use on a drug-eluting stent, but failed to come up with the combinations claimed in the 1997 patents or find a solution to the problem of restenosis. (Rogers Decl. at A5-A6 ¶13, A26-A33 ¶¶ 61-75, A70 ¶181, A71-A72 ¶186; Mikos Decl. at A100 ¶36, A73-A74 ¶207). Even though the drugs used showed promise in animal models, that failed repeatedly to translate into a successful clinical outcome in humans when used on a stent. (Rogers Decl. at A26-A33 ¶¶ 61-75).

For example, Medtronic attempted to develop a drug-eluting stent in the early-to-mid 1990s, as reflected by numerous Medtronic patents, including the Berg '650 patent that BSC relies on so heavily upon as well as the Tuch '411 patent and the Wolff '208 patent cited in BSC's motion. (D.I. 263, BSC Br. at 13 n. 7; A1078-A1084; A1134-A1146; A1098-A1111).

REDACTED

[3] *See also* Pharmacol & Therapeutics 2001; 92:165-178 at 167, (A1611) ("[r]estenosis remains a major limitation in the long-term success of PTCA" and "[e]arly trials with numerous pharmacological and mechanical devices have been disappointing"); Teirstein *et al.* at 1996-1997, (A2378-A2379) ("[s]ince the late 1970s, mammoth efforts and resources have been directed to restenosis" and "[s]cores of devices, hundreds of drugs, and innumerable revascularization 'strategies' have failed to eliminate the 10%-50% risk of recurrence after angioplasty") (A2378-A2380); (Rogers Decl. at A13-A14 ¶¶ 39-43); (Mikos Decl. at A155-

REDACTED Perhaps this was because the Berg patent focused on the drug dexamethasone, not a rapamycin drug, and the use of a biodegradable polymer, not a nonerodable polymer. In any event, Medtronic was unable to introduce its own drug-eluting stent (the Endeavor stent) in the United States until 2008, long after the success of Cypher® and some 15 years after the Berg patent was filed. The Endeavor stent does not use the approaches described in Berg or the other the Medtronic patents cited by BSC, but instead uses the invention claimed in the 1997 patents, including a rapamycin drug in a nonerodible polymer coating.

Guidant (now part of Abbott, which makes the Xience/Promus stent), also tried and failed numerous times to develop a successful drug-eluting stent.

REDACTED

Later, Guidant picked up its efforts and focused on the development of a stent using the drug Actinomycin-D. (Rogers Decl. at A27-A28 ¶¶62-63;

REDACTED

That stent failed spectacularly in clinical trials, resulting in a halt to both the trials and Guidant's Actinomycin-D development program. (Rogers Decl. at A27-A28 ¶ 63;

REDACTED

Desperate to develop a drug eluting stent, Guidant next attempted to develop a paclitaxel-eluting stent without a polymer coating in conjunction with another company, Cook Inc. That stent also failed and was never commercialized. (Rogers Decl. at A28 ¶ 64;

REDACTED

After the remarkable success of the Cypher® stent,

A156 ¶¶ 199-202).

and its inability to develop its own drug eluting stent, Guidant adopted Cordis's invention claimed in the 1997 patents – the use of a rapamycin drug in a nonerodible, fluorinated polymer on stents, released in a controlled manner over several weeks. (Rogers Decl. at A58-A61 ¶¶ 144-155; **REDACTED**

Many other companies such as Biocompatibles, Jomed, Quanum, and BiodivYsio attempted to develop drug-eluting stents using drugs such as dexamethasone, 7-hexanolyltaxol, tacrolimus, batimastat, 17-β-estradiol, and pimecrolimus, none of which are analogs of sirolimus. (Rogers Decl. at A26-A33 ¶¶ 61-75;

REDACTED

All of these efforts failed. *Id.*

Finally, BSC itself engaged in an extensive research program to develop a drug-eluting stent. This program ultimately resulted in the Taxus paclitaxel stent, which was introduced after the Cypher® stent and is not at issue in these actions.

REDACTED

Over time, clinical studies demonstrated that BSC's Taxus stent was clinically inferior to the Cypher® stent and that many cardiologists preferred rapamycin drugs to paclitaxel. (Rogers Decl. at A44-A46 ¶¶ 108-113;

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4. Skepticism In The Art About The Claimed Polymer/Drug Stents

Although the use of nonerodible polymers on drug-eluting stents is well-established now, that was not always the case. In 1997, many opinion leaders and researchers were highly

skeptical about the use of nonerodible polymer/drug coatings for stents, believing that such polymers would cause unacceptable inflammation in the coronary artery that would persist indefinitely. For example, leading researches from the Thoraxcenter, University of Rotterdam, Cleveland Clinic, and Mayo Clinic published a 1996 article in *Circulation* reporting that a variety of nonabsorbable and biodegradable polymers all caused significant levels of inflammation. They concluded by warning against the use of polymers as a stent coating:

> The present study demonstrates the marked inflammatory and neointimal response to an array of biodegradable as well as nonbiodegradable polymers after implantation in the porcine coronary artery. ***This reaction must be fully understood before we can make use of these or other polymers as implant materials in stents or drug delivery devices.***[4]

This was not an isolated view, but was held by many researchers and reflected in numerous articles. (Mikos Decl. at A97-A100 ¶¶ 31-34). Based on this concern, the general view in 1997 was that if one were to use a polymer on a stent, one should use a *bioabsorbable* polymer because it will break down and not be permanently present in the artery to cause inflammation indefinitely. (Mikos Decl. at A99-A100 ¶¶ 34-35; Rogers Decl. at A69-A70 ¶¶ 179-180). This view is reflected in (among other things) Medtronic's Berg patent, which teaches that "a bioabsorbable polymer is probably more desirable" than a nonerodable polymer "since, unlike a biostable polymer, it will not be present long after implantation to cause any adverse, chronic tissue response." (A1082, 4:39-42; Mikos Decl. at A100 ¶35; Rogers Decl. A70 ¶ 180).

[4] van der Giessen *et al.*, Marked Inflammatory Sequelae to Implantation of Biodegradable and Nonbiodegradable Polymers in Porcine Coronary Arteries, *Circulation* 1996; 94(7):1690-1697 at 1696, (A2441).

5. The Development And Stunning Success of The Cypher® Stent Embodying the Claimed Inventions

Out of all of the innumerable possibilities for a restenosis treatment, the inventors of the 1997 Patents came up, for the first time, with the combination of elements that led to the Cypher® stent. These elements, including a rapamycin drug, the use of nonerodible polymers (including fluorinated polymers and acrylates), and coating them on a stent to achieve controlled elution over a period of several weeks, are claimed in the 1997 patents. The Cordis inventors proceeded to develop their invention into what ultimately became the Cypher® stent. Cordis began an initial trial of the Cypher® stent in humans in 1999, referred to as the "First-in-Man" trial. This was the first test of any drug-eluting stent in a human to treat restenosis.

The results, published in 2001, surprised nearly everyone. (Rogers Decl. at A52-A58 ¶¶ 132-143). They exceeded all prior expectations, including those of the inventors, the study investigators, and other cardiologists who learned of the results. (Rogers Decl. at A52-A54 ¶¶ 133-137). The Cypher® stent did not simply make incremental progress in treating restenosis, it almost completely eliminated the problem. (Rogers Decl. at A34-A40 ¶ 81-94). In an article published in the prestigious journal *Circulation*, the reaction of leading cardiologists was summed up in "the now fabled words spoken by Patrick Serruys," a world-renowned cardiologist, who after viewing intravascular ultrasound images of sirolimus-eluting stents said simply, "If I am in a dream, please don't wake me."[5]

The astonishing results of the First-In-Man trial led to the near immediate adoption of the Cypher® stent by interventional cardiologists following FDA approval, resulting in over $1 billion dollars in revenue in the first 8 months following its April 2003 launch. (Rogers Decl. at A50 ¶ 126). With the advent of the Cypher® stent, in-stent restenosis changed from a chronic

disease to a preventable illness. (Rogers Decl. at A55 ¶ 140) Patients with coronary artery disease who received the Cypher® stent no longer needed repeat hospital visits, resulting in a marked improvement in their quality of life, and significant reductions in the risk of death, heart attack, or repeat stenting or bypass surgery of the same artery. (Rogers Decl. at A55 ¶¶ 140-141).

6. The Prior Art Relied Upon By BSC

a. The Berg Patent

BSC selects as its primary reference the Berg '650 patent filed in 1993 and assigned to Medtronic. As noted above, the Berg patent is one of several Medtronic patents resulting from its failed drug-eluting stent program. The Berg patent described a manufacturing process for making drug eluting stents, consisting of dissolving a drug and polymer in a solvent and applying the solution to a stent. Berg included in his patent specification a long laundry list of drugs and drug classes that could possibly be used in the process described, which includes thousands of possible drugs. (A1083, 5:19-40; Mikos Decl. at A104-A105 ¶¶ 51-52). Table 1 of the patent listed a several individual drugs – dexamethasone, dexamethasone phosphate, vitamin E, aspirin, and heparin – as suitable drugs. (A1082, Table 1). The individual examples all used dexamethasone. (A1083-A1084, 5:43-7:15). No mention was made of any rapamycin drug. Nothing in the Berg patent suggests that rapamycin would be more likely to succeed for use on a drug eluting stent than any of the thousands of other potential drugs in his laundry list.

As for polymers, the Berg patent contained a laundry list that spanned half a column of the specification and included at least dozens of polymers that could potentially be used. (A1082, 4:43-5:7). Berg '650, however, narrowed down this laundry list by directing the person

[5] Teirstein *et al.* at (A2378).

of ordinary skill to bioabsorbable polymers, explaining that "a bioabsorbable polymer is probably more desirable since, unlike a biostable polymer, it will not be present long after implantation to cause any adverse, chronic local response." (A1082, 4:39-42). Consistent with this direction, all of the specific examples in Berg used either no polymer or a bioabsorbable polymer. (A1083-1084, 5:43-7:15). The Berg patent is consistent with the prevailing wisdom at the time that nonabsorbable polymers were to be avoided. (Mikos Decl. at A100 ¶ 35).

b. The Morris Patent

The Morris '781 patent is one of the many references before 1997 showing success of a drug in treating restenosis in animal models. The Morris '781 patent reflects work done by Dr. Randall Morris of Stanford University in 1991 in conjunction with American Home Products ("AHP") demonstrating that rapamycin, which had previously been shown to have anti-fungal and immunosuppressive properties, also prevented restenosis when tested in rats.[6] In all of his experiments, rapamycin was delivered systemically. The Morris patent further states that it is preferred that rapamycin be administered starting three days before the angioplasty procedure. (A1095, 8:17-49; A1096, 10:17-34). This, of course, would not be possible using a stent, which is introduced at the time of the procedure.

Dr. Morris included in his specification a list of numerous possible methods of administering rapamycin, including: in solid carriers such as a powders or tablets; in liquid carriers such as solutions, suspensions emulsions syrups, elixirs and pressurized compositions administered orally, intravenously, or by intramuscular, interperitoneal or subcutaneous injection; in the form of a conventional suppository; as an aerosol for administration by

[6] The Morris '781 patent and other patents stemming from the same research are assigned to co-plaintiff Wyeth (AHP's successor) and exclusively licensed to Cordis. Wyeth and Cordis have

intranasal or intrabronchial inhalation or insufflation; transdermally through the use of a transdermal patch using a cream, ointment, paste, gel or occlusive device such as a semipermiable membrane covering a reservoir containing the drug; topically as a solution cream or lotion; or via an intravascular stent impregnated with rapamycin. (A1096-A1097, 10:35-11:50). Other than the systemic administration described in the examples, the Morris patent does not describe a preferred method among the various other modes of administration.

c. The Skotnicki Patent

The Skotnicki '286 patent represents work done by AHP to develop derivatives of sirolimus primarily for use as an in immunosuppressive drug for transplant patients. (Mikos Decl. at A129 ¶¶ 119-121). Although the Skotnicki patent describes these derivatives as being "useful as immunosuppressive, antiinflammatory, antifungal, antiproliferative, and antitumor agents" (A1086, 1:64-67), it focuses on their immunosuppressive properties. (Mikos Decl. at A129 ¶ 121). It describes tests used to evaluate the "[i]mmunosuppressive activity" of the described compounds (A1087, 4:6-67), and explains that they "are useful in the treatment or inhibition of transplantation rejection" and a variety of other immune and inflammatory conditions (A1088, 5:43-56). No specific tests are described for restenosis or neointimal proliferation. (Mikos Decl. at A129 ¶ 121). The patent describes a variety of different ways of administering the compounds, but does not include stent delivery. (A1088-A1089, 6:3-7:34).

LEGAL STANDARDS

SUMMARY JUDGMENT

Summary judgment may not be granted unless "there is no genuine issue as to any material fact." Fed. R. Civ. P. 56(c). In determining whether summary judgment is appropriate,

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accused the Xience/Promus stent of infringing certain of these patents in other pending litigation.

the "evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986).

The trial court's duty at the summary judgment motion stage of the litigation is merely to discern "whether there are disputed material facts"; it does not extend to resolving any such disputes. *SunTiger, Inc. v. Scientific Research Funding Group*, 189 F.3d 1327, 1333 (Fed. Cir. 1999). If the factual evidence leaves "room for some difference of opinion," the accused infringer has failed to meet the clear and convincing standard at summary judgment. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1575 (Fed. Cir. 1987). Moreover, in considering summary judgment, a District Court "can and should take into account expert testimony, which may resolve or keep open certain questions of fact." *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 427 (2007).

OBVIOUSNESS

In *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734 (2007) ("*KSR*"), the Supreme Court re-affirmed that the obviousness determination is based on the underlying factual inquiries outlined in *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966) – the scope and content of the prior art; differences between the prior art and the claims at issue; and the level of ordinary skill in the art. The Court also reaffirmed that "secondary considerations" such as "commercial success, long felt but unsolved needs, failure of others, etc." may "give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Id.*

The Supreme Court further explained that a patent can be granted on a combination of elements and that such a patent "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. In resolving

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See Civil Action No. 08-230-JAP-TJB (D. N.J.)

whether such a combination is obvious, it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* As the Supreme Court emphasized, a "factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." *Id.* at 421; *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000).

ARGUMENT

MATERIAL ISSUES OF DISPUTED FACT EXIST RELATING TO THE SCOPE AND CONTENT OF THE PRIOR ART.

Under *Graham*, the scope and content of the prior art is a critical factual inquiry underlying the obviousness analysis, and a material factual dispute precludes summary judgment. *See KSR,* 550 U.S. at 427 (summary judgment is appropriate when "the content of the prior art, the scope of the patent claim, and the level of ordinary skill in the art is not in dispute, and the obviousness of the claim is apparent in light of these factors"). *See also Andersen Corp. v. Pella Corp.*, 300 Fed. Appx. 893, 896-97 (Fed. Cir. 2008) (finding a "genuine issues of material fact exists as to the scope and content of the prior art" precluding summary judgment).

1. Factual Disputes Exist Concerning What The Berg Patent Would Have Taught A Person Of Ordinary Skill In 1997

The Berg patent is the central piece of BSC's obviousness defense, but BSC offers nothing besides attorney argument as to what the Berg patent would have taught (or not taught) a person of ordinary skill in the art and how it would have been understood and interpreted in light of the knowledge available in the art. Cordis provides expert declarations that directly contradict BSC's attorney argument, creating genuine issues of material fact as to each of the three key teachings of Berg: what Berg taught at the time of the invention about what polymer might be successful for use in a drug-eluting stent, what drug might be successful for use in a drug-eluting stent, and the appropriate release characteristics.

a. Appropriate Polymers

All of the asserted claims of the 1997 patents require the use of a nonerodible polymer coating on the stent, and certain claims require fluorinated and/or acrylate-based nonerodable polymers. BSC argues that the Berg patent would have taught a person of ordinary skill in 1997 to use a nonabsorbable polymer and specifically an acrylate-based or fluorinated polymer. D.I. 263, BSC Br. at 11, 27-28. BSC provides no expert declaration or other evidence from the perspective of a person of ordinary skill in 1997 to support this assertion, but instead relies solely on attorney argument.

Cordis's expert has offered opinions that squarely contradict BSC's attorney assertions. As Dr. Mikos explains in his declaration, the Berg '650 patent would not have directed a person of ordinary skill in 1997 to the use of nonabsorbable polymers. (Mikos Decl. at A106 ¶ 54). To the contrary, when combined with the then-existing skepticism in the art about polymer inflammation, Berg '650 would have directed a person of ordinary skill to use a biodegradable polymer instead. (Mikos Decl. at A100 ¶ 35, A107 ¶ 55, A144 ¶ 173).

The opinions of Dr. Mikos are amply supported by the art he cites and the language of the Berg '650 patent itself, which cautioned that a biodegradable polymer is "probably more desirable" because it will degrade. Berg went on to express the concern that a nonerodable polymer will "be present long after implantation" to cause "adverse, chronic local response" in the artery. (Mikos Decl. at A107 ¶ 55; A1082, 4:37-42). Consistent with this warning, all of the examples of the Berg patent either used no polymer or used a biodegradable polymer. (Mikos Decl. at A107-A108 ¶ 56; A1082, 4:37-42). As Dr. Mikos further explains, the long laundry list of possible polymers in Berg would provide little guidance to a person of ordinary skill. (Mikos Decl. at A106 ¶ 54). He concludes that a person of skill reading the Berg patent in 1997 would

have been discouraged from using the type of polymer claimed in the 1997 patents. At a minimum, there is a material issue of fact and summary judgment should be denied.

b. Appropriate Drugs

The claims of the 1997 patents require a rapamycin or macrocyclic lactone analog thereof. Disputed issues of material fact also exist concerning the teachings of the Berg patent that bear on this claim limitation. BSC asserts (again only with attorney argument) that Berg "teaches the use of anti-inflammatory, anti-proliferative, and anti-restenotic agents." D.I. 263, BSC Br. at 3-4. But as Dr. Mikos explains, Berg does nothing more than describe extremely broad categories among a long laundry list of possible drugs that could include most drugs known to humankind. (Mikos Decl. at A104-A105 ¶¶ 51-52). Dr. Mikos further opines that there is no guidance or direction of any kind in Berg as to what broad category of drugs should be selected, much less any focus on those drugs that are structurally or functionally similar to sirolimus. As Dr. Mikos further explains, the Berg patent actually directs the person of ordinary skill toward drugs that are very different from the rapamycin family, including dexamethasone, heparin, aspirin, and Vitamin E.[7] (Mikos Decl. at A107-A108 ¶ 56-57; A1082, Table 1; A1083-A1084, Examples 1-7.)

c. Controlled Release

The claims of the 1997 patents require "controlled release" of the drug from a nonerodible polymer coating (or a fluorinated or acrylate-based polymer coating) "over a period

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Dr. Rogers's accompanying declaration explains that although significant efforts were made in the prior art to test anti-proliferative drugs, this categories nevertheless encompassed an enormous number of possibilities, and other classes of drugs were also of interest to researchers, as demonstrated by the different classes of drugs tested in clinical trials. (Rogers Decl. at A67 ¶

of several weeks." (Mikos Decl. at A90-A91 ¶ 10). BSC asserts (yet again relying only on attorney argument) that a person of skill would appreciate this from Berg, pointing to "general statements" in the Berg patent stating that an "object of the present invention" is to "allow for sustained release of the drug to vascular tissue," and that the release rate can be controlled "by varying the ratio[] of drug to polymer." D.I. 263, BSC Br. at 12. But Dr. Mikos contradicts this argument, opining that a person of ordinary skill would not have known or understood from Berg that the release characteristics set forth in the claims of the 1997 patents should be employed. (Mikos Decl. at A108 ¶ 58). The Berg statements provide no time frame and do not say whether release occurs over hours, days, or weeks. (*Id.*) BSC also points to Example 6, but that describes release of dexamethasone from a specific ***biodegradable*** polymer (poly(L-lactic acid)), and even then for only a period of 10 days. (D.I. 263, BSC Br. at 12; A1083, 6:34:48; A1079, Figure 1; Mikos Decl. at A108 ¶ 58). As Dr. Mikos explains, a person of ordinary skill would not understand these portions of Berg to teach the controlled release of a drug from a nonerodable polymer (much less a fluorinated or acrylate-based polymer) over a period of several weeks. (Mikos Decl. at A108-A109 ¶ 58-59).

2. Factual Disputes Exist Concerning What The Morris Patent Would Have Taught A Person Of Ordinary Skill In 1997

A second prior art reference relied on by BSC is the Morris patent, but as to the teachings of this patent and how it would be understood by a person of ordinary skill, BSC again presents nothing but attorney argument. BSC lifts the statement from the Morris patent that rapamycin could be delivered via a stent to argue that it would be "particularly obvious" to do so. D.I. 263, BSC Br. at 13, 27. As Dr. Mikos explains, however, all of the examples of the Morris patent involve systemic delivery, and stent delivery was only mentioned as part of a long discussion

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that included many possible ways of delivering rapamycin. (Mikos Decl. at A126 ¶ 109). Thus, as Dr. Mikos explains, the Morris patents would not have directed a person of ordinary skill in 1997 toward the use of stent delivery more than any of the other methods of administration described in the patent. (Mikos Decl. at A125-A126 ¶ 107, 109) Factual disputes therefore exist concerning what the Morris patent would have taught to a person of ordinary skill in 1997 about delivery of rapamycin.

There is also a factual dispute as to whether the Morris patent described controlled release of rapamycin from a stent over a period of several weeks. BSC asserts that the "Morris patent discloses that the treatment should last for 13 or more days following PTCA." D.I. 263 BSC Br. at 14. But, as Dr. Mikos explains, this statement is lifted from a portion of the patent describing *systemic* delivery, and would not be understood by a person of ordinary skill as describing controlled release from a stent over a period of several weeks. (Mikos Decl. at A126 ¶ 110)[8]

3. BSC Admits That The Relevant Prior Art Goes Beyond The Berg, Morris And Skotnicki Patents, And This Prior Art Creates Additional Issues of Fact

BSC tries to make its obviousness defense out to be a "simple" case of combining only 2-3 references. D.I. 263, BSC Br. at 21. BSC's own opening brief, however, belies this and actually relies on many additional references to make its obviousness case. Many factual disputes exist concerning the scope and content of these references, as with the Berg and Morris patents.

[8] Factual disputes also exist concerning the scope and content of the Skotnicki patent. Dr. Mikos opinions that it would not have taught a person of ordinary skill in 2001 to use of the disclosed drugs in the context of the present inventions – treating rapamycin via a nonerodible polymer-coated stent. (Mikos Decl. at A172, ¶¶ 122-123.)

For example, BSC relies on ***seven*** additional references to try to show, in combination with the Berg patent, that it was "well known to a person of ordinary skill in the art in April of 1997" that the polymers claimed in the 1997 patents "were particularly useful as coatings [in] blood-contacting implantable devices." D.I. 263, BSC Br. at 28. That, however, is a vigorously disputed question of fact. As Dr. Mikos explains, a person of ordinary skill in 1997 would have believed based on the Berg patent as well as other prior art that nonabsorbable polymers (such as those claimed in the 1997 patents) would likely be problematic because they would cause inflammation when used as a coronary stent coating. (Mikos Decl. at A97-A100 ¶¶ 31-35). The disputed nature of this question, as well as the number of different prior art references that bear on it, renders it inappropriate for determination on summary judgment.

Similarly, BSC cites to three further references in addition to the Morris patents for the proposition that rapamycin would have been "particularly obvious" to employ in the stents of Berg. D.I. 263, BSC Br. at 27. Again, this is a fact issue, and Cordis has offered contrary expert testimony. As Dr. Mikos explains, in 1997 rapamycin was only one of a very large number of possible drugs that were being considered and could have been used that showed some success in animal models. (Mikos Decl. at A144-A145 ¶¶ 173-174.)

BSC also cites five additional patents "disclosing polymeric coated stents that are designed to locally deliver a therapeutic agent to treat restenosis." D.I. 263, BSC Br. at 13 n. 7. As Dr. Mikos explains, however, many of these additional patents, including the Tuch patent, the Wolff patent and the Dayton patent, teach the use of biodegradable polymers and teach away from the nonabsorbable polymers claimed in the 1997 patents. (Mikos Decl. at A119 ¶ 88, A122 ¶ 97, A124 ¶103). This is a disputed issue of fact as well.

4. <u>Factual Disputes Exist About Whether The Prior Art Taught Away From The Claimed Inventions</u>

Beyond the many factual disputes concerning the teachings of the individual references relied on by BSC, there are additional factual disputes as to whether the prior art teaches away from the inventions claimed in the 1997 patents. In *KSR*, the Supreme Court emphasized the importance of "teaching away" in the obviousness analysis. *KSR*, 550 U.S. at 1739-1740 ("when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious."). The factual disputes here preclude summary judgment.

A prior art reference "teaches away" from the claimed invention "when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *DePuy Spine, Inc. v. Medtronic Sofamar Danek, Inc.*, 567 F.3d 1314 (Fed. Cir. 2009). In other words, there is a teaching away where prior art references "'criticize, discredit, or otherwise discourage' investigation into the invention claimed." *Id.* Whether the prior art teaches away from the claimed inventions is a question of fact. *Ortho-McNeil v. Teva,* Nos. 2008-1549, 2008-1550, 2009 WL 2604919 at *4 (Fed. Cir. Aug. 26, 2009).

Determining whether a reference teaches away from the claimed invention involves drawing inferences as to what a person of ordinary skill would understand the reference to teach at the time of the invention—an exercise particularly inappropriate on a motion for summary judgment. Summary judgment is even more inappropriate in this case because Cordis has submitted an uncontroverted declaration from an acknowledged expert explaining that a person of ordinary skill in 1997 would have understood the reference in question as teaching away from the claimed invention. In such cases, the Federal Circuit has found summary judgment improper. *See Ortho-McNeil* at *3 (reversing summary judgment of obviousness because expert

testimony that the prior art taught away from the claimed combination "raises material questions of fact as to whether a skilled artisan would have found the claimed combination...to be obvious"); *Andersen*, 300 Fed. Appx. at 896-99 (reversing summary judgment of obviousness, because there was evidence in the record that prior art references "taught away from using" one of the elements in the claimed combination).

As Dr. Mikos explains, many prior art references discouraged, and therefore taught away from, the use of the claimed nonerodable polymers as a stent coating. (Mikos Decl. at A97-A100 ¶¶ 31-35). As noted above, leading researchers in the prestigious journal *Circulation* reported that a variety of polymers demonstrated "marked inflammatory and neointimal response," and warned that "this reaction must be fully understood biologically before we can make use of these or other polymers as implant materials in stents or drug delivery devices." *Circulation* 1996;94(7) at 1696, (A2441). Another 1997 article explained that "a number of polymers, although biocompatible in other settings, excite an extensive inflammatory response when implanted in porcine coronary arteries." *Cardio Res* 1997;35(3) at 410, (A1415). Many other researchers expressed this concern as well.[9] (Mikos Decl. at A97-A100 ¶¶ 31-35). Thus, as Dr. Mikos explains, if a person of ordinary skill in 1997 wanted to use a polymer coating, they would be encouraged to select a *biodegradable* polymer because it will break down and

[9] *See, e.g.*, Rechavia *et al.*, Biocompatibility of polyurethane-coated stents: tissue and vascular aspects. *Catheterization and Cardiovascular Diagnosis* 1998; 45(2):202-207, at pp. 202-203, 205-206; Orloff *et al.*, Biodegradable implant strategies for inhibition of restenosis. *Advanced Drug Delivery Reviews* 1997; 24:3-9, at pp. 3-4, 8; Wilczek *at al.*, Comparison of self-expanding polyethylene terephthalate and metallic stents implanted in porcine iliac arteries. *Cardiovascular Intervent Radiol* 1996; 19:176-180, at pp. 176, 178, 180; Murphy *et al.*, Percutaneous polymeric stents in porcine coronary arteries. Initial experience with polyethylene terephthalate stents. *Circulation*, 1992;86(5):1596-1604, at pp. 1596, 1698, 1602-1603.

disappear over time. (Mikos Decl. at A97-A100 ¶¶ 31-35). They would be discouraged from using a nonerodable polymer because it would be present forever to cause inflammation. (*Id.*)

Teaching away considerations are especially powerful in this case because the primary prior art reference relied on by BSC contains explicit language discouraging the use of nonabsorbable polymers, as claimed in the 1997 patents. As Dr. Mikos explains, the Berg patent discourages and criticizes the use of nonerodible polymers because they will "be present long after implantation" to cause "adverse, chronic local response." (Mikos Decl. at A107 ¶ 55; A1082, 4:37-42). Berg further teaches that nonerodible polymers could only be used if they have "a relatively low chronic tissue response." (Mikos Decl. at A107 ¶ 55; A1082, 4:54-55). Consequently, Berg teaches that "a bioabsorbable polymer is probably more desirable," and all of the examples provided use either no polymer or a bioabsorbable polymer. (Mikos Decl. at A107-A108 ¶¶ 55-56; A1082, 4:37-42; A1083-A1084, 5:45-7:15).

Similar teachings appear in other prior art references cited by BSC. For example, The Tuch patent, filed two years after the application that issued as the Berg patent, contains the same statements criticizing and discouraging the use of nonabsorbable polymers. (A1142, 5:17-22). The Wolff '208 patent teaches that "[c]ontrolled release, via a *bioabsorbable* polymer, offers to maintain the drug level within the desired therapeutic range for the duration of the treatment (A1109, 7:53-55 (emphasis added)), and that "[t]he compound which is preferred is a polyphosphate ester," a bioabsorbable polymer (A1109, 8:26-27), which is "a superior drug delivery system for a prosthesis" (A1110, 9:20-23).

Courts have relied on exactly this type of teaching away as evidence of non-obviousness. For example, in *Andersen*, the Federal Circuit held that the patent owner provided sufficient evidence of nonobviousness to overcome summary judgment when it "submitted into the record

prior art references that taught away from using the [prior art] TWP mesh as an insect screen" because they "teach that the TWP mesh possessed many characteristics that an ordinary skilled insect screen designer would have viewed as undesirable. 300 Fed. Appx. at 897-98. Similarly here, Cordis has introduced abundant evidence that persons of ordinary skill would have viewed the use of the claimed nonerodible polymers as undesirable as a coating for a drug-eluting coronary stent based on teachings in the prior art.

Similarly, in *Ortho-McNeil v. Teva*, the Federal Circuit concluded that material issues of fact precluding summary judgment arose from expert testimony that two German references taught away from the claimed fixed-dosage tablets. 2009 WL 2604919 at *3. The expert explained that the German references "emphasize the flexibility in choosing combinations and doses of medications based on individual needs" and that "the claimed fixed-dosage combination tablet was disparaged in the German references and disfavored in the art at the time." Similarly here, the prior art, including the Berg patent, emphasized the advantages of biodegradable polymers and nonerodable polymers were disparaged and disfavored. (Mikos Decl. at A97-A100 ¶¶ 31-35).

BSC concedes that the Berg '650 patent "expresses a preference for bioabsorbable polymers," but argues that this does not constitute "teaching away." D.I. 263, BSC Br. at 27. The cases BSC relies on, however, do not support its position. For example, in *DePuy Spine*, the Court found that a cited prior art reference "teaches away" from the claimed invention involving a rigidly-locked screw for spinal surgery because it "warns that rigidity increases the likelihood that the screw will fail within the human body" and expresses a preference for a screw without this feature. *Id.* 567 F.3d at 1313-14. The teaching in Berg '650 and other references is exactly this type of disclosure – it warns that the use of nonabsorbable polymers has the potential to

cause "adverse, chronic, local response," a response that would render the resulting polymer coated drug eluting stent ineffective for restenosis prevention.[10]

Moreover, even if a particular prior art reference does not technically "teach away," it is nonetheless relevant to the obviousness inquiry. The Federal Circuit has recognized that the "general skepticism of those in the art – not amounting to teaching away – is also 'relevant and persuasive evidence' of nonobviousness." *See Monarch Knitting*, 139 F.3d. at 885 (citing *Gillette*, 919 F.2d at 720)).

Summary judgment is particularly inappropriate in this case where Cordis has offered expert declarations based on the scientific literature at the time and contemporaneous documents showing that a person of ordinary skill in the art would understand that the prior art teaches away from the approach claimed in the 1997 patents. BSC offers only attorney argument. But on summary judgment, the Court must resolve all ambiguities and draw all reasonable inferences against the moving party. *Ortho-McNeill v. Mylan*, 520 F.3d 1358, 1360-61 (Fed. Cir. 2008). BSC's motion should be denied.

5. Factual Disputes Exist Concerning What The Prior Art Taught as a Whole

Yet another factual dispute aside from the teachings of individual pieces of prior art concerns the teaching of the prior art as a whole at the time of the claimed inventions. The teaching of the prior art "as a whole" can be an important factor in an obviousness analysis. *See Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1358 (Fed. Cir. 1997)

[10] The other cases cited by BSC do not provide a contrary result. In *Dystar Textilfarben Gmbh & Co. v. C.H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006), the court merely found that the *absence* of a teaching in the prior art references was alleged to constitute "a teaching away." *Id.* at 1364-65. In *Alza v. Andrx Pharms., LLC*, 607 F. Supp. 2d 614, 637-38 (D. Del. 2009), perceived advantages of certain dosage regimens were alleged to suggest that other dosage regimens would not work. In contrast, here, Berg '650 contains specific language that warns of the adverse effects of using nonabsorbable polymer as a stent coating.

(analyzing obviousness based on prior art "as a whole"); *Ortho-McNeil v. Mylan*, 520 F.3d at 1365 (considering whether invention was obvious "in light of the evidence available at the time of the invention"). In determining obviousness, it is important to consider "the nature of the choices available to one skilled in the art, the specificity of the prior art, and the predictability of results in the area of interest." *Ortho-McNeil v. Teva*, 2009 WL 2604919 at *3.

BSC's obviousness analysis focuses on a tiny slice of the prior art. BSC makes no attempt to consider the myriad of alternatives available to the person of ordinary skill in 1997, the difficulty and complexity involved in trying to sort through and reconcile them, the numerous failures and false starts, the many conflicting opinions about what approaches showed promise, and the inherent unpredictability of the field. Instead, using hindsight based on the success of the claimed inventions, they combine snippets of prior art to try to retrace the path taken by the inventors. This is improper. As the Federal Circuit explained, it is "always inappropriate" for an accused infringer to "simply retrace[] the path of the inventor with hindsight, discount[ing] the number and complexity of the alternatives, and conclud[e] that the [claimed invention] was obvious." *Ortho-McNeil v. Mylan*, 520 F.3d at 1364. Although in hindsight the "pathway to the invention" may "seem to follow the logical steps," the "inventor's insights, willingness to confront and overcome obstacles, and yes, even serendipity, cannot be discounted" in the obviousness analysis. *Id.*

BSC's consideration of the prior art as a whole is limited to its factual assertion that the prior art taught "a clear preference for the local delivery of therapeutic agents to treat restenosis." D.I. 263 at 31. This factual assertion, however, is vigorously contested. BSC cites selected documents and deposition testimony to support its view, but BSC ignores the significant

evidence pointing the other way.[11] As Dr. Rogers explains, in 1997 a huge number of different systemically delivered therapies were considered for addressing restenosis. (Rogers Decl. at A19-A26 ¶¶ 56-60). Some researchers believed local drug delivery showed more promise while others believed the same about systemic drug therapy.[12] The persistent belief in the promise of systemic drug therapy, even after the claimed inventions, is demonstrated by a massive clinical trial conducted in as late as 2002 to evaluate the systemic use of the drug tranilast to treat restenosis, involving approximately 11,500 patients and costing approximately $100 million. (Rogers Decl. at A25). Others, **REDACTED** believed that radiation was the most promising approach. (Rogers Decl. at A17 ¶ 50; **REDACTED** Thus, there was no clear guidance in 1997 as to whether systemic administration, local drug delivery, or some other method (like radiation) would ultimately prove successful.

In its brief, BSC cites to no expert testimony on any of these important factual questions. Indeed, BSC provides no evidence whatsoever on how a person of ordinary skill would have

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understood the prior art "as a whole" in 1997. Resolution of these factual disputes is the province of the jury. Summary judgment is inappropriate.

BSC'S ARGUMENTS OF MOTIVATION TO COMBINE AND REASONABLE EXPECTATION OF SUCCESS RAISE MATERIAL FACT DISPUTES

1. Material Factual Disputes Abound In BSC's "Motivation to Combine" Arguments

Under *KSR*, motivation to combine references remains an important consideration in assessing obviousness. *See Ortho-McNeil v. Mylan*, 520 F.3d at 1365 (after *KSR*, "a flexible [teaching, suggestion or motivation] test remains the primary guarantor against a non-statutory hindsight analysis"). In this case, it is particularly important because BSC is relying primarily on specific bits and pieces of references from a vast array of relevant prior art, which provides the person of ordinary skill with almost infinite possible combinations. BSC has the burden of proving that the person of ordinary skill would have been motivated to select particular references and then further to combine pieces of them to make the claimed invention.

The Federal Circuit has repeatedly held that "[t]he presence or absence of a motivation to combine references in an obviousness determination is a pure question of fact." *Alza Corp. v. Mylan Labs.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006) (citations omitted) (cited by BSC). *See Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 381 F.3d 1371, 1378 (Fed. Cir. 2004) ("Whether the prior art provide the suggestion or motivation or teaching to select from prior knowledge and combine it in a way that would produce the invention at issue is a question of fact"); *Monarch Knitting,* 139 F.3d at 882 ("th[e] evidence creates a genuine issue as to whether those of ordinary skill would have had a motivation to combine"); *Girafa.com,* 2009 WL 2949509 at *1; *Oxford Gene Technology Ltd. v. Mergen Ltd.*, 345 F. Supp. 2d 444, 455 (D. Del. 2004) (denying summary judgment of obviousness because genuine issues of material fact

existed as to whether the skilled person would have been motivated to combine the teachings of the prior art).

a. Motivation to Combine Pieces of the Berg and Morris Patents

BSC bases its obviousness defense on the assertion that the person of ordinary skill in the art would have been motivated to combine bits and pieces of the Berg '650 and Morris '781 patents to arrive at the claimed inventions. (For particular claims, BSC tries to throw in numerous other references.) Cordis has submitted expert declarations explaining in detail why, at the time of the invention, the person of ordinary skill would not have been motivated to make the patented combination. These assertions raise numerous material factual disputes.

BSC asserts that motivation to make the claimed invention is provided by "Berg's disclosure that 'any therapeutic substance' is appropriate." D.I. 263, BSC Br. at 25-26. But as Drs. Mikos and Rogers explain, there were a huge number of different therapeutic substances that were being considered to treat restenosis. (Mikos Decl. at A104-A105, A145 ¶¶ 51-52, 173; Rogers Decl. at A19-A33, A71 ¶¶ 56-75, 185). Berg itself identifies drug classes comprising thousands of potential drugs, and focuses specifically on dexamethasone, tocopherol, vitamin E, and heparin. The specification never mentions any rapamycin drug, any similar drug, or even any immunosuppressive drug. (Mikos Decl. at A105, ¶52). As Dr. Mikos explains, there is nothing in Berg that would motivate a person of ordinary skill to look outside the thousands of drugs described in the Berg patent and choose a rapamycin drug, which is never described or suggested.[13] (Mikos Decl. at A144, ¶ 174). At a minimum, a disputed issue of fact exists.

[13] Nor does the disclosure in Berg of "anti-inflammatory agents" among the laundry list of possible drugs provide any real motivation select a rapamycin drug. "Anti-inflammatory agents" are still a very large class of drugs covering an enormous number of compounds. Notably, Medtronic was never able to parlay Berg '650's teachings of "any therapeutic agent" or "anti-inflammatory agents" into a successful drug-eluting stent. (Mikos Decl. at A18 ¶ 50; Rogers

BSC next argues that the person of ordinary skill would have been motivated to combine the selected portions of the Berg and Morris patents because of "[t]he common purpose of the inventions disclosed in these two patents" – provision of an anti-restenotic therapy. D.I. 263, BSC Br. at 25. But the mere identification in the prior art of knowledge of a problem and motivation to solve it is insufficient to prove motivation to combine. *See Innogenetics v. Abbott Labs.*, 512 F.3d 1363, 1373 (Fed Cir. 2008). A huge number of references existed proposing wide-ranging approaches to providing an anti-restenotic therapy, from systemic drugs, to catheters, to radiation, to lasers, to a variety of stent-related approaches. (Mikos Decl. at A104-A106, A145 ¶¶ 51-52, 173; Rogers Decl. at A13-A33 ¶¶ 39-75). Drs. Mikos and Rogers opine that neither the prior art as a whole or the individual references provide a motivation as to why these two references, out of the thousands that describe potential solutions for restenosis, should be combined. (Mikos Decl. at A143-A145 ¶¶ 171-175; Rogers Decl. at A62-A65, A67 ¶¶ 158-166, 173, 187). A material issue of disputed fact exists.

BSC argues that the motivation to make the claimed combination is further supported by the disclosure in the Morris patent that rapamycin is appropriate for treating restenosis in animal models and that rapamycin "can be administered intravascularly or via a vascular stent impregnated with rapamycin." D.I. 263, BSC Br. at 26. As Dr. Mikos explains, however, the Morris patent describes a myriad of different routes of administration, and all of the examples involve systemic delivery. (Mikos Decl. at A125 ¶ 107). Nothing in Morris would lead one to select the approach described in the Berg patent rather than either the systemic delivery mode which was the preferred route of administration in Morris or any one of the many other routes of administration described in the Morris patent. (Mikos Decl. at A125 ¶ 107).

Decl. at A63 ¶¶ 159-160).

Moreover, even if one were to select the Berg and Morris patents from the multitude of prior art, there is a fact issue as to whether a person of ordinary skill, in the absence of hindsight, would be motivated to combine the many different approaches suggested in the precise manner that would make the claimed combination. To establish obviousness, BSC must demonstrate that a person of ordinary skill would have been motivated to combine the elements "in the way the claimed new invention does." *KSR*, *550* U.S. at 418. Substantial evidence (including expert declarations) shows that a person of ordinary skill in 1997 considering Berg and Morris would be motivated to use a biodegradable polymer which Berg describes as "more desirable" and uses in all of its examples, rather than nonerodible polymers which it disparages because they can "be present long after implantation" to cause "adverse, chronic local response." (Mikos Decl. at A107, ¶ 55; A1082, 4:37-38.) There is also substantial evidence that no motivation would exist to select fluorinated polymers or acrylate-based polymers from the long laundry list of polymers described. And, substantial evidence exists that nothing in either Morris or Berg would motivate a person of ordinary skill to provide controlled release of a rapamycin drug from a nonerodible polymer (or a fluorinated or acrylate-based polymer) over a period of several weeks, as claimed in the 1997 patents. (Mikos Decl. at A107, ¶ 56.)

BSC also points to the specification of the 1997 patents as providing a motivation to combine the Berg and Morris patents. D.I. 263, BSC Br. at 26. But "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992). BSC cannot eliminate fact issues by relying on the inventors own patent as to provide a motivation not found in the prior art.

b. Alleged Motivation Based on Other Prior Art Cited by BSC

Although BSC purports to rely only on the Berg, Morris and Skotnicki patents, it actually points to other prior art to try to establish a motivation to combine. BSC cites various articles on the use of rapamycin systemically in animal studies to argue that rapamycin would have been "a particularly obvious drug" to combine with Berg. But all of these references concern systemic delivery of rapamycin. (Mikos Decl. at A144-A145 ¶ 174.) They provide no motivation to a person of ordinary skill reading the Berg patent to use rapamycin instead of the many drugs taught in the Berg patent itself, or to select rapamycin from the large number of compounds that had shown some promise in animal studies. (*Id.*)

BSC also points to various references describing the use of acrylate polymers and flouropolymers on various medical devices other than stents. D.I. 263, BSC Br. at 28. But there is nothing in these references that would suggest the use of these specific polymers on stents, or suggesting that they should be used in lieu of the biodegradable polymers taught as preferred by Berg. (Mikos Decl. at A106, ¶¶ 54). These additional references raise further fact issues for the jury.

c. Whether There Were a Finite Number of Predictable Solutions to the Problem of Restenosis

The Supreme Court in *KSR* identified as another factual issue to be considered in assessing obviousness is whether there is a "finite number of identified, predictable solutions" to the problem addressed by the invention. *KSR Int'l Co.* 550 U.S. at 421. The Federal Circuit has also identified "predictability" as "a touchstone of obviousness." *DePuy*, 567 F.3d at 1326. Here, the proposed solutions were neither finite nor predictable – the references BSC relies on alone include laundry lists of thousands of possible drugs and polymers leading to a virtually infinite number of possible combinations. As Drs. Mikos and Rogers explain, in 1997 the there

were not a finite number of identified solutions to the problem of restenosis in 1997. (Mikos Decl. at A155-A157 ¶ 199-203; Rogers Decl. at A13-A14 ¶¶ 39-43). To the contrary, persons of ordinary skill were faced with a multitude of possible therapeutic approaches and a multitude of possible drug and polymer combinations. (Mikos Decl. at A155-A157 ¶¶ 199-203; Rogers Decl. at A13-A14 ¶¶ 39-43).

Additionally, these proposed solutions were anything but predictable. (Rogers Decl. at A68 ¶ 176). Researchers in the field had little idea which, if any, would prove successful. (Mikos Decl. at A143-A144 ¶¶ 171-172; Rogers Decl. at A68 ¶ 176). This is demonstrated by the fact that time and time again researchers tried an approach which had shown promise in animal models, only to see it join the "wasteland" of failed efforts to treat restenosis. (Mikos Decl. at A156 ¶ 201; Rogers Decl. at A26, A58 ¶¶ 61, 146; Teirstein *et al.* at 1996, (A2378)). As Dr. Mikos explains, the reaction of particular devices, drugs and polymers to the environment of the coronary artery following angioplasty was highly complex and unpredictable. (Mikos Decl. at A96-A97 ¶¶ 26-27). Major medical device companies such as Medtronic and Guidant tried and failed. (Rogers Decl. at A64, A70 ¶¶ 163, 181). And, the results of the claimed invention when realized on the Cypher® stent stunned the interventional cardiology field and was a spectacular commercial success. (Mikos Decl. at A148-A154 ¶¶ 183-195; Rogers Decl. at A48-A58 ¶¶ 122-143). If the claimed invention was obvious and predictable in 1997, why didn't anyone else come up with it over the years and years of repeated failed efforts to deal with this intractable problem?

BSC contests the fact that the prior art presented the person of ordinary skill with a multitude of possible approaches and combinations. Once again, Cordis's position is based on detailed expert declarations supported by persuasive reasoning, whereas BSC's position is based

entirely on attorney argument. At a minimum, there is a disputed question of material fact, and thus BSC's motion should be denied.

2. Cordis Documents and Testimony Cited by BSC Raise Factual Disputes

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That is true for every combination patent. A patent on a combination of elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. Moreover, BSC ignores other portions of this evidence which undercut its argument, such as the statements that Cypher® "challenge[d] conventional thinking" and that the inventors faced significant challenges, including determining "[w]hich was the right drug," whether "a single drug" could "prevent neointimal hyperplasia," whether a drug could "stop restenosis or only delay it" and whether a drug-eluting stent could "successfully compete with radiation therapy—the major focus at the time." Ex. 76. This evidence as a whole raises additional disputed issues of fact.

3. BSC's "Reasonable Expectation of Success" Arguments Also Raise Fact Issues

The "presence or absence of a reasonable expectation of success from making" a particular combination of prior art references is "a pure question of fact." *Alza*, 464 F.3d at 1289. Improperly using the 1997 patents' specifications as its starting point, BSC's attorneys argue that the skilled person would have had "a reasonable expectation of success when combining Berg and Morris." *See, e.g.*, D.I. 263, BSC Br. at 26. Once again, apart from attorney

argument and vague allegations of "expect[ation], BSC presents no affirmative evidence of how or why the skilled would have had a reasonable likelihood of success of arriving at the claimed inventions. In contrast, Cordis has submitted expert and documentary evidence that shows that in 1997 there was considerable skepticism about whether a nonerodible polymer-coated drug eluting stent would solve the problem of restenosis. (Mikos Decl. at A99 ¶ 34; Rogers Decl. at A69 ¶ 179).

Moreover, BSC's arguments that the results were predictable and expected is flatly inconsistent with assertions made by BSC in its briefs to this Court urging the invalidity of the claims on grounds of enablement and written description. BSC itself characterizes the invention as "the application of an unpredictable technology in the early stage of development." D.I. 263, BSC Br. at 19. BSC repeatedly characterizes the field as "highly unpredictable." D.I. 263, BSC Br. at 2, 3, 17, 21. Furthermore, BSC admits that the field was new at the time of the invention because there were no drug-eluting stents for human use available in the market as of the critical dates. (D.I. 258, BSC Br. at 30.) BSC's own statements show that there are disputed issues of fact concerning predictability of the claimed inventions.[14]

NUMEROUS FACT DISPUTES CONCERNING THE "OBJECTIVE INDICIA" OF NONOBVIOUSNESS EVIDENCE PRECLUDE SUMMARY JUDGMENT

BSC almost completely ignores the powerful "real world" objective indicia of nonobviousness in this case. As the Federal Circuit has "repeatedly explained," evidence of objective indicia of nonobviousness "is not just cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of non-obviousness." *Ortho-McNeil*

[14] BSC argues that 1997 Patent specifications and file histories do not "include any statements" that the results of the claimed inventions would have been unexpected." D.I. 263, BSC Br. at 26-27. But there is no requirement that unexpected results of the claimed invention be described in the specification or file history.

Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1365 (Fed. Cir. 2008). Evidence of objective indicia "'may often be the most probative and cogent evidence [of non-obviousness] in the record.'" *Procter & Gamble Co.*, 566 F.3d at 998. Such evidence may frequently establish that an invention appearing to have been obvious in light of the prior art was not. *See e.g., Alco Std. Corp. v. Tennessee Valley Authority*, 808 F.2d 1490, 1499-1501 (Fed. Cir. 1986).

In this case, the objective evidence establishes that in 1997 the particular claimed inventions – described by BSC in hindsight as "simple combinations" – were neither "simple" nor "predictable" nor "obvious" to persons of ordinary skill:

- Commercial Success – The Cypher® stent has been a spectacular commercial success. Eight months following FDA approval, it generated over $1 billion in sales, and caused a dramatic shift in the stent market. Sales of bare-metal stents dropped by nearly $600 million dollars as physicians switched to using Cypher®. Cypher® also dramatically expanded the market as a whole for stents, causing the U.S. stent market to balloon to $1.927 billion in sales, with Cypher® accounting for over $1 billion of this revenue. A nexus exists between the commercial success and the claimed inventions because the Cypher® stent embodies those inventions, and the commercial success resulted from the Cypher® stent's employment of the claimed inventions.

  The Xience/Promus stents also embody the inventions of the 1997 patents have also been a commercial success since receiving FDA approval in July of 2008.

- Long-Felt Need and Failure of Others – Restenosis was a long-standing problem for years before the claimed inventions. Many different approaches to the problem were tried and failed, including polymer-drug coated stents, prior to the Cypher® stent, none of the approaches was ever used to create a clinically or commercially successful drug eluting stent. Prior to and after the availability of the Cypher® stent, the efforts of numerous medical device manufacturers to develop a drug-eluting stent for the prevention of restenosis ended in failure.

- Unexpected Results - The dramatic clinical results of the Cypher® stent were highly unexpected. The Cypher® stent did not simply make incremental progress in treating restenosis – the initial reports indicated that it had almost completely eliminated the problem. These results were highly unexpected and stunned the cardiology community. The claimed combinations were important to these results.

- Adoption by Others/Copying - Following the groundbreaking success of Cypher® and after its stent attempts failed, Abbott's predecessor Guidant, designed its own stent, the Xience V stent, that used the invention of the 1997 patents, including a rapamycin drug, a nonabsorbable fluorinated polymer, and controlled release over several weeks. In clinical trials, the Xience™ stent replicates the effectiveness of the Cypher® stent in preventing restenosis.

  Despite its Taxus stent, BSC recognized the need for a stent with a rapamycin drug that used the claimed inventions of the 1997 patents, and agreed with Abbott to market a private label version Xience called the Promus stent. Medtronic introduced the Endeavor stent which uses the invention claimed in the 1997 patents. Thus, three out of the four stents currently sold in the U.S. have adopted the approach used in Cypher®, and claimed in the patents-in-suit.

- Industry Acclaim - Beginning with the availability of the FIM clinical trial results, the Cypher® stent was immediately hailed as a ground-breaking product by cardiologists and others throughout the industry. The industry acclaim and recognition received by the Cypher® stent was the result of its highly unexpected and remarkable clinical results, which in turn was due to the inventions of the patents-in-suit.

(Mikos Decl. at A148-A162 ¶¶ 182-212; Rogers Decl. at A13-A61 ¶¶ 39-155).

What is particularly noteworthy in this case is that, for strategic reasons, BSC has elected not to contest any of the secondary considerations for purposes of this motion and thus they must be considered uncontested. This alone warrants the denial of summary judgment. Recognizing that it has no answer to this argument, BSC simply waves aside this powerful, real world evidence of nonobviousness and asks the Court to ignore it completely. D.I. 263, BSC Br. at 39-40. That is contrary to the law. An "analysis of obviousness *must* address objective indicia of nonobviousness, if any." *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 725 (Fed. Cir. 1999) (emphasis in original).

BSC cites several cases in which a court found obviousness despite assertions of secondary considerations of nonobviousness. None of those cases, however, is applicable here. Virtually all of BSC's cases involve determinations of obviousness ***after trial*** – not summary judgment. *See e.g., Leapfrog Enters., Inc. v. Fisher-Price, Inc.* 485 F.3d 1157 (Fed. Cir. 2007);

Agrizap, Inc. v. Woodstream Corp., 520 F.3d 1337 (Fed. Cir. 2008); *Asyst Techs., Inc. v. Emtrak, Inc.*, 544 F.3d 1310 (Fed. Cir. 2008); *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318 (Fed. Cir. 2008); *Richardson-Vicks Inc. v. The Upjohn Co.*, 122 F.3d 1476 (Fed. Cir. 1997); *Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757 (Fed. Cir. 1988).[15] And, none involves a situation, as here, where the evidence of secondary considerations is overwhelming and is undisputed for purposes of a summary judgment motion.

CORDIS'S STATEMENTS IN THE *DING* CASE AND THE *INTER-PARTES* REEXAMINATION DO NOT OBVIATE THE MANY DISPUTED ISSUES OF MATERIAL FACT

BSC relies on statements taken out of context from the unrelated litigation, *Boston Scientific Scimed, Inc. v. Cordis Corp.*, Case No. 03-283-SLR (D. Del.) (the "Ding case"), involving BSC's U.S. Patent No. 6,120,536 to Ding *et al.*, ("Ding '536") as evidence of obviousness. BSC Br. at 35-38. The claimed inventions of the 1997 patents are completely different from the Ding patent. The obviousness question in that case concerned the use of a topcoat, and the statements quoted by BSC were made in the context of addressing a very different issue. The Ding patent did not mention anything about rapamycin or any particular drug. Moreover, the statements merely confirmed that the technology required to coat a stent with a polymer was known prior to the Ding patent. That is no more than what is disclosed by the Berg patent and other patents cited by BSC. Cordis *did not say* that the particular combinations claimed in the 1997 patents would have been obvious to a person of ordinary skill.

BSC's reliance upon the ongoing *inter partes* reexaminations of the 1997 patents is also misplaced. *See* D.I. 263, BSC Br. at 16-17, 38-39. To date, the Patent Office has merely issued first office actions largely parroting back the combinations made by Abbott. No final office

[15] In the only summary judgment decision, *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714 (Fed.

action has been issued. The reexamination still must proceed through a final action, post-final proceedings, and an appeal before the Board of Patent Appeals before it exits the Patent Office, a process that will likely take many years. The Federal Circuit has held that non-final determinations in inter partes reexaminations are of "little relevance ... on the factual issues underlying the question of obviousness." *Callaway Golf Co. v. Acushnet Co.*, 576 F.3d 1331, 1343 (Fed. Cir. 2009).

CONCLUSION

Because BSC's motion raises numerous disputed issues of material fact, summary judgment should be denied.

ASHBY & GEDDES

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Cir. 1991), unlike here, many of the primary *Graham* factors were not in dispute.

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Dated: October 9, 2009

CERTIFICATE OF SERVICE

I hereby certify that on the 19th day of October, 2009, the attached **REDACTED PUBLIC VERSION OF DEFENDANTS/COUNTER-PLAINTIFFS JOHNSON & JOHNSON AND CORDIS'S OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT OF INVALIDITY OF THE '7286, '3286, AND '473 PATENTS-IN-SUIT PURSUANT TO 35 U.S.C.§ 103** was served upon counsel of record at the address and in the manner indicated:

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